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Qualitative Models of Neural Activity and the Carleman Embedding Technique

A thesis

presented to

the faculty of the Department of Mathematics

East Tennessee State University

In partial fulfillment

of the requirements for the degree

Master of Science in Mathematical Sciences

by

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August 2009

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Keywords: Carleman Embedding, Fitzhugh Nagumo, Green Function, Excitability

ABSTRACT

Qualitative Models of Neural Activity and the Carleman Embedding Technique

by

Azamed Yehuala Gezahagne

The two variable Fitzhugh Nagumo model behaves qualitatively like the four variable Hodgkin-Huxley space clamped system and is more mathematically tractable than the Hodgkin Huxley model, thus allowing the action potential and other properties of the Hodgkin Huxley system to be more readily be visualized. In this thesis, it is shown that the Carleman Embedding Technique can be applied to both the Fitzhugh Nagumo model and to Van der Pol's model of nonlinear oscillation, which are both finite nonlinear systems of differential equations. The Carleman technique can thus be used to obtain approximate solutions of the Fitzhugh Nagumo model and to study neural activity such as excitability.

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DEDICATION

To my daughter

Sarah Azamed

ACKNOWLEDGMENTS

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1 INTRODUCTION

The theory of differential equations is a basic tool in physics, engineering, biology and other mathematically related sciences. In particular, numerous natural laws and models of natural phenomenon are described by nonlinear finite autonomous systems of differential equations

$$\frac{d\mathbf{u}}{dt} = \mathbf{V}(\mathbf{u}, t).$$

Examples are the Van der Pol's equations, Fitzhugh Nagumo equations, Lorenz model, and Lotka Volterra models [2]. These models described different biological problems on different scales. However, because of the nonlinear nature of the system, it is quite complicated to find the closed form of the solution of the above system.

In 1932, Torsten Carleman, motivated by an idea of Henri Poincare in response to a challenge by David Hilbert, proposed a method of embedding a finite dimensional system of nonlinear differential equations where \mathbf{V} is analytic in \mathbf{u} into an infinite system of linear differential equations [7].

After 30 years, Bellman and Richardson pointed out the idea of Carleman linearization method to approximate the solution of nonlinear differential equations [8]. After Bellman and Richardson, numerous authors studied a method of Carleman embedding in connection with finding approximate solution of nonlinear system of differential equations [2]. From the historical development of the Carleman embedding technique, it has become an effective tool in the study of nonlinear dynamical systems.

The purpose of this thesis is to show that the Carleman embedding technique can be used to approximate the solution of Van der Pol's equation and Fitzhugh Nagumo

model. Moreover, it is shown that the technique can be applied to explore neural activity such as excitability. The organization of the thesis is as follows. Section 2 defines Carleman embedding scheme and discusses the technique applied on Van der Pol's equation. Comparison between numerical solution and Carleman solution of the Van der Pol's equation has been done. In section 3, we introduces the Hodgkin Huxley and Fitzhugh Nagumo Neural Models. Mathematical analysis of the Carleman embedding technique to Fitzhugh Nagumo model is also presented in detail. Section 4 is devoted mainly on simulation results of the Carleman embedding technique applied on Fitzhugh Nagumo models. Comparison between the solutions obtained by the numerical method and the Carleman technique of the Fitzhugh Nagumo equation has been done. It also discusses the idea of equilibrium points, suprathreshold and subthreshold nature of the action potential.

2 CARLEMAN EMBEDDING TECHNIQUE

2.1 Introduction

The purpose of this section is the analysis of the Carleman embedding technique and its application to finite dimensional systems of nonlinear differential equations. In particular, we consider Van der Pol's equation.

Before describing the application of the technique, we first recall the general scheme of Carleman linearization. Consider the system with analytic nonlinearities

$$\frac{d\mathbf{u}}{dt} = \mathbf{V}(\mathbf{u}, \mathbf{t}) \quad (1)$$

where

$$\mathbf{V} : R^k \times R \rightarrow R^k$$

and \mathbf{V} is analytic in \mathbf{u} .

We should mention that the original Carleman approach [7] dealt with autonomous polynomial systems (1). Following Carleman we define the function

$$u_{\mathbf{n}}(t) = \prod_{i=1}^k (u_i(t))^{n_i} \quad (2)$$

where $\mathbf{u}(t)$ satisfies (1) and $\mathbf{n} \in Z_+^k$. Here Z_+^k denotes k-tuples of nonnegative integers.

The system (1) implies the following linear differential-difference equation

$$\frac{d\mathbf{u}}{dt} = \sum_{\mathbf{n}' \in Z_+^k} M_{\mathbf{n}\mathbf{n}'}(t) u_{\mathbf{n}'}. \quad (3)$$

Note that the differential-difference equation (3) is finite order only in the case of \mathbf{V} polynomial in \mathbf{u} . It should also be noted that in the case of autonomous systems

(1) the coefficient matrix $M_{nn'}$ is constant. In view of the fact that the set Z_+^k is countable, one finds easily that (3) is equivalent to an infinite dimensional system of linear differential equations. Obviously, the solution of the system (1) is linked to the solution of (3) by

$$u_i = u\mathbf{e}_i, i = 1, \dots, k$$

where $\mathbf{e}_i = (0, \dots, 0, 1_i, 0, \dots, 0)$ is unit column vector. So the finite dimensional non-linear systems (1) is embedded into the infinite dimensional linear system (3). Such an embedding is called the **Carleman embedding** [2].

2.2 Carleman Embedding on Van der Pol's Equation

The Van der Pol equation, proposed by Balthasar van der Pol in 1920 as a model of relaxation oscillations with nonlinear damping, is governed by the second order differential equation

$$\frac{d^2x}{dt^2} - \epsilon(1 - x^2)\frac{dx}{dt} + x = 0$$

where x is the dynamical variable and ϵ is a small parameter [5, 6]. When ϵ is small, the quadratic term x^2 is very small and the system becomes a linear differential equation with a negative damping. Thus, the fixed point ($x = 0, \frac{dx}{dt} = 0$) is unstable (an unstable focus when $0 < \epsilon < 2$ and an unstable node, otherwise). On the other hand, when x is large, the term x^2 becomes dominant and the damping becomes positive. Therefore, the dynamics of the system is expected to be restricted in some area around the fixed point. Actually, the van der Pol system satisfies Liénard's theorem ensuring that there is a stable limit cycle in the phase space. The van der Pol system is therefore a Liénard system [5, 6].

Using *Liénard's transformation* $y = x - \frac{x^3}{3} - \frac{1}{\epsilon} \frac{dx}{dt}$, the above equation can be rewritten as

$$\begin{aligned}\frac{dx}{dt} &= y + \epsilon\left(x - \frac{1}{3}x^3\right) \\ \frac{dy}{dt} &= -x\end{aligned}\tag{4}$$

which can be regarded as a special case of the **FitzHugh-Nagumo model** (also known as **Bonhoeffer-van der Pol model**) [13].

By using Maple, one can easily generate a numerical solution of the initial valued problem (4). For $x(0) = \alpha = 1$, $y(0) = \beta = 0$ and $\epsilon = 0.001$, we get the plot in Figure 1.

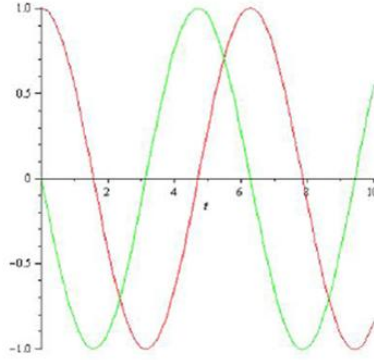


Figure 1: Numerical Solution of Van der Pol's equation for $\epsilon = 0.001$

To get an approximate solution to the above systems of finite nonlinear equations, we apply the Carleman embedding technique and solve in terms of an infinite set of linear equations as follows. Following the scheme proposed by Carleman and truncating at $n = 3$, we set

$$v_1 = x$$

$$v_2 = y$$

$$v_3 = x^2$$

$$v_4 = xy$$

$$v_5 = yx$$

$$v_6 = y^2$$

$$v_7 = x^3$$

$$v_8 = x^2y$$

$$v_9 = yx^2$$

$$v_{10} = xy^2$$

$$v_{11} = yx^2$$

$$v_{12} = yx^2$$

$$v_{13} = y^2x$$

$$v_{14} = y^3$$

Applying the derivatives of each v_i 's followed by substituting and rearranging the equations, we get

$$\begin{aligned}
\frac{dv_1}{dt} &= \frac{dx}{dt} = y + \epsilon x - \frac{\epsilon}{3}x^3 = v_2 + \epsilon v_1 - \frac{\epsilon}{3}v_7 \\
\frac{dv_2}{dt} &= \frac{dy}{dt} = -x = -v_1 \\
\frac{dv_3}{dt} &= \frac{dx^2}{dt} = 2x(y + \epsilon x - \frac{\epsilon}{3}x^3) = 2v_4 + 2\epsilon v_3 \\
\frac{dv_4}{dt} &= \frac{d(xy)}{dt} = x(-x) + y(y + \epsilon x - \frac{\epsilon}{3}x^3) = -v_3 + \epsilon v_5 + v_6 \\
\frac{dv_5}{dt} &= \frac{d(yx)}{dt} = x(-x) + y(y + \epsilon x - \frac{\epsilon}{3}x^3) = -v_3 + \epsilon v_5 + v_6 \\
\frac{dv_6}{dt} &= \frac{dy^2}{dt} = -2yx = -2v_5 \\
\frac{dv_7}{dt} &= \frac{dx^3}{dt} = 3x^2(y + \epsilon x - \frac{\epsilon}{3}x^3) = 3v_8 + 3\epsilon v_7 \\
\frac{dv_8}{dt} &= \frac{d(x^2y)}{dt} = (-x)^3 + 2yx(y + \epsilon x - \frac{\epsilon}{3}x^3) = -v_7 + 2\epsilon v_{11} + 2v_{13} \\
\frac{dv_9}{dt} &= \frac{d(yx^2)}{dt} = (-x)^3 + 2yx(y + \epsilon x - \frac{\epsilon}{3}x^3) = -v_7 + v_{10} + 2\epsilon v_{11} + v_{12} \\
\frac{dv_{10}}{dt} &= \frac{d(xy^2)}{dt} = x(-2yx) + y^2(y + \epsilon x - \frac{\epsilon}{3}x^3) = -2v_9 + \epsilon v_{13} + v_{14} \\
\frac{dv_{11}}{dt} &= \frac{d(yx^2)}{dt} = (-x)^3 + y(2yx + 2(y + \epsilon x - \frac{\epsilon}{3}x^3)) = -v_7 + 2\epsilon v_{11} + 2v_{12} \\
\frac{dv_{12}}{dt} &= \frac{d(xy^2)}{dt} = xy(-x) + y(-x^2 + y^2 + \epsilon yx) = -v_8 - v_{11} + \epsilon v_{13} + v_{14} \\
\frac{dv_{13}}{dt} &= \frac{d(xy^2)}{dt} = x(-2yx) + y^2(y + \epsilon x - \frac{\epsilon}{3}x^3) = -2v_9 + \epsilon v_{13} + v_{14} \\
\frac{dv_{14}}{dt} &= \frac{dy^3}{dt} = -3y^2x = -3v_{13}
\end{aligned}$$

One can write the above linear system of equations in the matrix form as

$$\frac{dV}{dt} = AV \quad (5)$$

where $V = [v_1, v_2, \dots, v_{14}]^T$ and

$$A = \begin{bmatrix} \epsilon & 1 & 0 & 0 & 0 & 0 & \frac{-\epsilon}{3} & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ -1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 2\epsilon & 2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -1 & 0 & \epsilon & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -1 & 0 & \epsilon & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 3\epsilon & 3 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -1 & 0 & 0 & 0 & 2\epsilon & 0 & 2 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -1 & 0 & 0 & 1 & 2\epsilon & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -2 & 0 & 0 & 0 & \epsilon & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & -1 & 0 & 0 & 0 & 2\epsilon & 2 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -1 & 0 & 0 & -1 & 0 & \epsilon & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -2 & 0 & 0 & 0 & \epsilon & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -3 & 0 \end{bmatrix}.$$

The solution to equation(5) is given by

$$V(t) = V_0 e^{At} \quad (6)$$

where V_0 is the initial value

$$V_0 = \begin{bmatrix} v_1(0) \\ v_2(0) \\ v_3(0) \\ v_4(0) \\ v_5(0) \\ v_6(0) \\ v_7(0) \\ v_8(0) \\ v_9(0) \\ v_{10}(0) \\ v_{11}(0) \\ v_{12}(0) \\ v_{13}(0) \\ v_{14}(0) \end{bmatrix} = \begin{bmatrix} x(0) \\ y(0) \\ x^2(0) \\ x(0)y(0) \\ y(0)x(0) \\ y^2(0) \\ x^3(0) \\ x^2(0)y(0) \\ x^2(0)y(0) \\ x(0)y^2(0) \\ x^2(0)y(0) \\ x(0)y^2(0) \\ x(0)y^2(0) \\ y^3(0) \end{bmatrix} = \begin{bmatrix} \alpha \\ \beta \\ \alpha^2 \\ \alpha\beta \\ \beta\alpha \\ \beta^2 \\ \alpha^3 \\ \alpha^2\beta \\ \alpha^2\beta \\ \alpha\beta^2 \\ \alpha^2\beta \\ \alpha\beta^2 \\ \alpha\beta^2 \\ \beta^3 \end{bmatrix}.$$

We now use Maple to plot the solution of Van der Pol's equation obtained by Carleman embedding technique. Figure 2 shows the result of Carleman Embedding for $x(0) = \alpha = 1, y(0) = \beta = 0$ and $\epsilon = 0.001$.

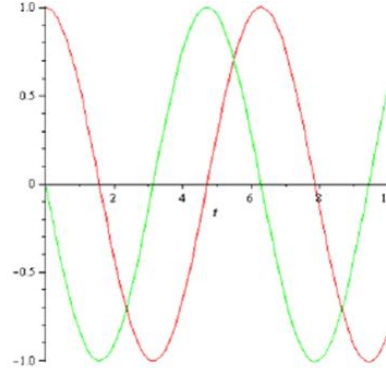


Figure 2: Solution by Carleman Embedding Technique for $\epsilon = 0.001$

Now we can compare the two results and it is shown that the Carleman embedding technique gives the best approximation to the solution of Van der Pol's equation. Figure 3 shows a comparison between the solutions obtained by Numerical method and Carleman Embedding technique.

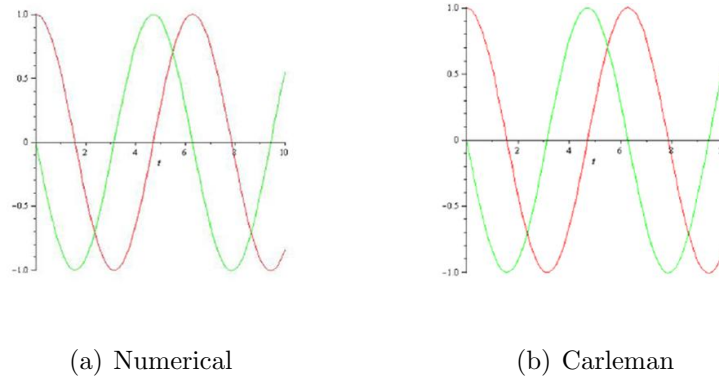


Figure 3: Comparison of Numerical and Carleman solutions

For large values of ϵ (such as $\epsilon = 0.1$), relaxation oscillation occurs. A. V. Hill stated that relaxation oscillations are the oscillations governing all periodic physiological phenomenon [9]. Figure 4 shows the relaxation oscillation when ϵ is large.

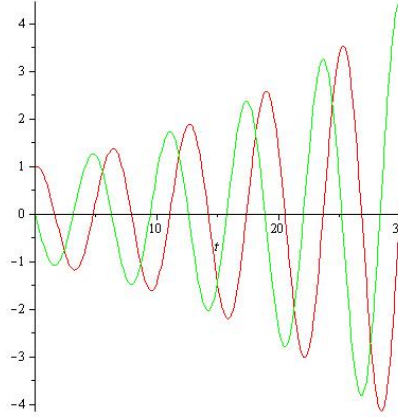


Figure 4: Solution by Carleman Embedding Technique for $\epsilon = 0.1$

2.3 Conclusion

These results illustrate the utility of the Carleman embedding technique to find solutions of systems of nonlinear differential equations. We get the same solution because Van der Pol's equations have periodic solutions. Carleman embedding technique can also be used to explain relaxation oscillation in Van der Pol's equations.

Carleman embedding technique did appear to have some practicality in the study of problems with periodic solution and I used the same technique to get solutions of systems of nonlinear differential equations which do not have solutions of a periodic nature, in particular the Fitzhugh Nagumo equations.

3 FITZHUGH NAGUMO MODEL

3.1 Introduction

One of the leading frontiers of biophysics is the study of neurophysiology, which only several decades ago spawned an understanding of the basic processes underlying the unique electro-chemical communication system that constitutes our nervous system. Our brains and every other subsystem in the nervous system are composed of cells called neurons [1].

While neurons tend to vary greatly in size, shape, and properties, such cells commonly share certain typical features. Anatomically, the cell body (soma) is the site at which the nucleus and major subcellular structures are located and is the central point from which synthesis and metabolism are coordinated [1].

A more prominent feature is a long tube-like structure called the axon whose length often exceeds 1 cm. It is known that the propagation of a nerve signal is electrical in nature; after being initiated at a site called the axon hillock, it propagates down the length of the axon to terminal branches, which form loose connections (synapses) with neighboring neurons. A propagated signal is called an action potential. A neuron has a collection of dendrite (branched, "root-like") appendages, which receive incoming signals by way of the synapses and convey them to the soma [1].

How the detailed electro-chemical mechanism operates is a fascinating story that, broadly speaking, is now well understood. It is known that neuronal signals travel along the cell membrane of the axon in the form of a local voltage difference across

the membrane. In the resting state, the cytoplasm (cellular fluid) inside the axon contains an ionic composition that makes the cell interior slightly negative in potential (-50mV difference) with respect to the outside. Such a potential difference is maintained at a metabolic expense to the cell by active pumps located on the membrane. These continually transport sodium ions (Na^+) to the outside of the cell and convey potassium ions (K^+) inwards so that concentration gradients of both species of ions are maintained. The differences in these and other ionic concentration across the membrane result in the net electric potential that is maintained across the membrane of the living cell. We take that the voltage V is the potential difference (inside minus outside) for the membrane [1].

Thinking of the axon as a long electrical cylindrical cable is a vivid but somewhat erroneous conception of its electrical properties. First, while a current is implied, it is predominantly made up of ionic flow (not electrons), and its direction is not longitudinal but transverse (into the cell). Second, while a passive cable has fixed resistance per unit length, an axon has an excitable membrane whose resistance to the penetration of ions changes as the potential difference V is variable [1].

The flow of charged ions across a cell membrane is restricted to the specific molecular sites called pores, which are scattered along the membrane surface. It is known that many different kinds of pores (each specific to a given ion) are present and that these open and close in response to local conditions including the electrical potential across the membrane [1]. This can be broadly understood in terms of changes in the conformation of the proteins making up these pores, although the biophysical details are not entirely known.

To understand the process by which an action potential signal is propagated, we must look closely at events happening in the immediate vicinity of the membrane. Starting the process requires a threshold voltage: the potential difference must be raised to about -30 to -20mV at some site on the membrane [1]. Experimentally this can be done by stimulating an electrode that pierces a single neuron. Biologically this happens at the axon hillock in response to an integrated appraisal of excitatory inputs impinging on the soma. As a result of reaching this threshold voltage, the following sequences of events occur [1].

1. Sodium channel open, letting Na^+ ions enter the cell interior. This causes the cell membrane potential to depolarize; i.e, the inside becomes positive comparing to the outside, the reverse of resting-state polarization
2. After small delay, the potassium channel open, letting K^+ leave the cell. This restores the original polarization of the cell membrane, and further causes an overshoot of the negative rest potential.
3. The sodium channels then close in response to a decrease in the potential difference.
4. Next to the site that experienced these events the potential difference exceeds the threshold level necessary to set in motion step 1. The process repeats, leading to spatial conduction of the spike-like signal. The action potential can thus be transported down the length of the axon without attenuation or change in shape. This makes a traveling wave [1].

3.2 Hodgkin-Huxley Model

Classically, it was known that the cell membrane carries a potential across the inner and outer surfaces, hence a basic model for a cell membrane is that of a capacitor and resistor in parallel [10]. The model equation takes the form

$$C_m \frac{dV}{dt} = -\frac{V - V_{eq}}{R} + I_{appl}$$

where C_m is the membrane capacitance, R the resistance, V_{eq} the rest potential, V the potential across the inner and outer surfaces, and I_{appl} represents the applied current. In landmark patch clamp experiments in the early part of the 20th century [10], it was determined that many cell membranes are excitable, i.e., exhibit large excursions in potential if the applied current is sufficiently large. Examples include nerve cells and certain muscle cells, e.g. cardiac cells [10].

From 1948-1952, Hodgkin and Huxley [10] conducted patch clamp experiments on the squid giant axon, a rather large part of nerve tissue suitable for experimentation given the technology of the time. Based on their experiments, they constructed a model for the patch clamp experiment in an attempt to give mathematical explanation for the axons excitable nature. A key part of their model's assumptions was that the membrane contains channels for potassium and sodium ion flow. In effect, the $\frac{1}{R}$ factor in the above equation became potential dependent for both channels. The underlying model equation is

$$C_m \frac{dV}{dt} = -[g_{Na}(V)(V - V_{Na}) + g_K(V)(V - V_K) + g_L(V - V_L)] \quad (7)$$

Here V_{Na} , V_K and V_L represent that part of the resting membrane potential that

is due to the contributions of the ions Na^+ , K^+ and L (all other mobile species) respectively.

It is generally assumed that g_L is independent of V , which is constant. To govern the ionic conductivities g_{Na} and g_K , it is necessary to introduce three variables n, m and h in the dynamics of the ionic pores. These hypothetical quantities could perhaps be interpreted as concentrations of proteins that must act in concert to open or close a pore. However, the equations were chosen to fit the data, not from a more fundamental knowledge of molecular mechanisms.

Hodgkin and Huxley defined

$$\begin{aligned} g_{Na} &= \bar{g}_{Na} m^3 h \\ g_K &= \bar{g}_K n^4 \end{aligned}$$

where the \bar{g} are constant conductivity parameters [10]. Hodgkin and Huxley [10] suggested that n, m , and h are voltage-sensitive gate proteins, that obey differential equations in which voltage dependence is described:

$$\begin{aligned} \frac{dn}{dt} &= \alpha_n(V)(1 - n) - \beta_n(V)n \\ \frac{dm}{dt} &= \alpha_m(V)(1 - m) - \beta_m(V)m \\ \frac{dh}{dt} &= \alpha_h(V)(1 - h) - \beta_h(V)h \end{aligned} \tag{8}$$

In addition, the quantities $\alpha_n, \alpha_m, \alpha_h, \beta_n, \beta_m, \beta_h$ are assumed to be voltage-dependent

as follows:

$$\begin{aligned}
\alpha_m(V) &= 0.1(V + 25)(e^{\frac{(V+25)}{10}} - 1)^{-1} \\
\alpha_h(V) &= 0.07e^{\frac{(V)}{20}} \\
\alpha_n(V) &= 0.01(V + 10)(e^{\frac{(V+10)}{10}} - 1)^{-1} \\
\beta_m(V) &= 4e^{\frac{V}{18}} \\
\beta_h(V) &= (e^{\frac{V+30}{10}} + 1)^{-1} \\
\beta_n(V) &= 0.125e^{\frac{V}{80}}
\end{aligned} \tag{9}$$

The values of other constants appearing in the equations are $\bar{g}_{Na} = 120$, $\bar{g}_K = 36$ and $g_L = 0.3mS/cm^2$; $V_{Na} = -115$, $V_K = 12$ and $V_L = -10.5989mV$.

Taken together, equations (8) and (9) represent a four-dimensional dynamical system (coupled ODEs) with highly nonlinear terms known as the Hodgkin-Huxley model. Because of the high nonlinear nature of the model, it is quite difficult to explore mathematically. Moreover, the internal variables m, n and h do not clearly relate to underlying molecular mechanisms [1].

It does however provide a basis for qualitative explanation of the formation of action potentials in the giant squid axon. Moreover, the model structure forms a basis for virtually all models of excitable membrane behavior. In the next section, we explore this model in the elegant way suggested by Fitzhugh and Nagumo [11, 12].

3.3 Fitzhugh Nagumo Model

The Fitzhugh-Nagumo equation is a simplification of the Hodgkin-Huxley model devised in 1952 [10]. The Hodgkin-Huxley has four variables and the Fitzhugh-Nagumo equation is a reduction of that model. The reduction is from four variables to two variables where phase plane techniques may be used for the analysis of the model.

The variables retained in the reduction of the model are the excitable variable and the recovery variable which are characterized as being the fast and slow variables respectively. FitzHugh explains that the model was devised in the same way as the Van der Pol equation [11]. Its solution does not, to be sure, give an accurate fit to curves obtained from many physical oscillators. The equation was intended, rather, to represent the qualitative properties of a wide class of such oscillators, while its algebraic form being chosen to be as simple as possible.

The purpose of the FitzHugh-Nagumo equation is to model the same phenomenon as the Hodgkin-Huxley model. The phenomenon that is modeled is the control of the electrical potential across a cell membrane. This control is due to the change of flow of the ionic channels of the cell membrane. This results in a change in potential which is used to send electrical signals between cells. This is readily observed in muscle and other excitable cells. For example the FitzHugh-Nagumo equation is used to model electrical waves of the heart [3].

The model is given by

$$\begin{aligned}\frac{dV}{dt} &= c(V - \frac{1}{3}V^3 + W + I(t)) \\ \frac{dW}{dt} &= -\frac{(V - a + bW)}{c}\end{aligned}\tag{10}$$

In these equations, the variable V represents the excitability of the system and could be identified with voltage (membrane potential in the axon); W is a recovery variable, representing combined forces that tend to return the state of the axonal membrane to rest. Finally, $I(t)$ is the applied stimulus that leads to excitation (such as input current) [11]. In typical physiological situations, such stimulus might be impulses, step functions, or rectangular pulses. Moreover, the variables a , b , and c are dimensionless and positive.

It is thus of interest to explore how equation (10) behaves when various functions $I(t)$ are used as inputs and we try to get the approximate solution to the above equations, particularly the action potential using the Carleman Embedding technique. Because of the nonlinearity nature of the model, we can not find the closed form of the solution. However, we can simulate and approximate. We can then use this to explore neural activity such as excitability.

3.4 One-Sided Green's Function

A one-sided Green's function relates the solutions of an inhomogeneous equation to the inhomogeneous term and the solutions of the corresponding homogeneous equation [4]. Green's functions have been determined for an extremely wide variety of differential equations.

Theorem 3.1 *If G is the solution of the homogeneous ($F(x) \equiv 0$) form of*

$$\frac{dX}{dt} = AX + F(t)$$

with $G(0) = \mathbf{1}$, then the solution to the inhomogeneous is

$$X(t) = X(0) + \int_0^t G(t-u)F(X)du.$$

Proof: If we take the derivative of $X(t)$, we get

$$\begin{aligned} \frac{dX}{dt} &= G(t-t)F(t) + \int_0^t \frac{dG}{dt}(t-u)F(X)du \\ &= \mathbf{1}F(t) + A \int_0^t G(t-u)F(X)du \\ &= AX + F(t) - AX(0). \end{aligned}$$

Let us assume that $X(0) = 0$ so that $AX(0) = 0$. Then

$$\frac{dX}{dt} = AX + F(t).$$

So a solution of the above nonhomogeneous system of differential equation is of the form

$$X(t) = \int_0^t G(t-u)F(t)du \tag{11}$$

If $X^*(t)$ is any other solution, then

$$\frac{d(X - X^*)}{dt} = A(X - X^*)$$

with $(X - X^*)(0) = 0$. This implies that $X = X^*$ and that equation (11) is a unique solution. ■

3.5 Carleman Embedding on Fitzhugh Nagumo Equation

Recall the F-N model:

$$\begin{aligned}\frac{dV}{dt} &= c(V - \frac{1}{3}V^3 + W + I(t)) \\ \frac{dW}{dt} &= -\frac{(V - a + bW)}{c}.\end{aligned}$$

Before we can apply Carleman embedding, we must transform the above Fitzhugh Nagumo equations. We can rewrite the above systems of equations as

$$\begin{aligned}\frac{dV}{dt} &= cV + cW + (cI - \frac{c}{3}V^3) \\ \frac{dW}{dt} &= \frac{-V}{c} - \frac{b}{c}W + \frac{a}{c} = \frac{-V}{c} - \frac{b}{c}(W - \frac{a}{b}).\end{aligned}$$

We can make the substitution

$$\theta = W - \frac{a}{b} \implies \frac{d\theta}{dt} = \frac{dW}{dt}.$$

Then the above equations can be written as

$$\begin{aligned}\frac{dV}{dt} &= cV + c\theta + c\frac{a}{b} + cI - \frac{c}{3}V^3 \\ \frac{d\theta}{dt} &= \frac{-1}{c}V - \frac{b}{c}\theta.\end{aligned}$$

One can write the above system in the matrix form as

$$\frac{dX}{dt} = AX + F(X) \tag{12}$$

where

$$A = \begin{bmatrix} c & c \\ \frac{-1}{c} & \frac{-b}{c} \end{bmatrix}, X = \begin{bmatrix} V \\ \theta \end{bmatrix}, F(X) = \begin{bmatrix} c\frac{a}{b} + cI - \frac{c}{3}V^3 \\ 0 \end{bmatrix}.$$

Let

$$G = \begin{bmatrix} g_{11} & g_{12} \\ g_{21} & g_{22} \end{bmatrix}$$

be the one-sided Green's function and let

$$\frac{dG}{dt} = AG ; G(0) = I_{2 \times 2}.$$

The solution of the above system is

$$G(t) = G(0)e^{At} = e^{At}.$$

Now using Theorem 2.1, we assume the solution of equation (12) is of the form

$$\begin{aligned} X(t) &= \int_0^t G(t-u)F(X)du \\ &= \int_0^t \begin{bmatrix} g_{11}(t-u) & g_{12}(t-u) \\ g_{21}(t-u) & g_{22}(t-u) \end{bmatrix} \begin{bmatrix} F_{11}(X) \\ 0 \end{bmatrix} du. \end{aligned}$$

So we have

$$X(t) = \begin{bmatrix} V(t) \\ \theta(t) \end{bmatrix} = \int_0^t \begin{bmatrix} g_{11}(t-u)F_{11}(X) \\ g_{21}(t-u)F_{11}(X) \end{bmatrix} du.$$

It follows that

$$\begin{aligned} V(t) &= \int_0^t g_{11}(t-u)F_{11}(V)du \\ &= \int_0^t g_{11}(t-u)[c\frac{a}{b} + cI - \frac{c}{3}V^3(u)]du \end{aligned}$$

and

$$\begin{aligned}\theta(t) &= \int_0^t g_{21}(t-u)F_{11}(V)du \\ &= \int_0^t g_{21}(t-u)\left[c\frac{a}{b} + cI - \frac{c}{3}V^3(u)\right]du.\end{aligned}$$

Now if we take the derivative of the above integral equations, we obtain

$$\begin{aligned}\frac{dV}{dt} &= g_{11}(t-t)\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(t)\right) + \int_0^t \frac{dg_{11}(t-u)}{dt}\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(u)\right)du \\ &= g_{11}(0)\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(t)\right) + \int_0^t \frac{dg_{11}(t-u)}{dt}\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(u)\right)du\end{aligned}$$

and

$$\begin{aligned}\frac{d\theta}{dt} &= g_{21}(t-t)\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(t)\right) + \int_0^t \frac{dg_{21}(t-u)}{dt}\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(u)\right)du \\ &= g_{21}(0)\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(t)\right) + \int_0^t \frac{dg_{21}(t-u)}{dt}\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(u)\right)du.\end{aligned}$$

Now we use Maple to find the components of matrix G and after some simplification

(Appendix 1) we can write

$$\begin{aligned}g_{11}(t) &= \frac{1}{2Q}[Ue^{xt} + Ve^{yt}] \\ g_{21}(t) &= \frac{1}{2Q}[e^{xt} - e^{yt}]\end{aligned}$$

where

$$\begin{aligned}
Q &= \sqrt{b^2 + 2bc^2 + c^4 - 4c^2} \\
U &= Q + c^2 + b \\
V &= Q - c^2 - b \\
x &= \frac{-b + c^2 + Q}{2c} \\
y &= \frac{-b + c^2 - Q}{2c}.
\end{aligned}$$

The derivatives of g_{11} and g_{21} are, respectively,

$$\begin{aligned}
g'_{11}(t) &= \frac{1}{2Q}[Uxe^{xt} + Vye^{yt}] \\
g'_{21}(t) &= \frac{1}{2Q}[xe^{xt} - ye^{yt}].
\end{aligned}$$

Now let us find the limit of the ratio of these two derivatives and the functions as

$t \rightarrow \infty$

$$\begin{aligned}
\lim_{t \rightarrow \infty} \frac{g'_{11}(t)}{g_{11}(t)} &= \lim_{t \rightarrow \infty} \frac{[Uxe^{xt} + Vye^{yt}]}{[Ue^{xt} + Ve^{yt}]} \\
&= \lim_{t \rightarrow \infty} \frac{Ux + Vye^{(y-x)t}}{U + Ve^{(y-x)t}} \\
\lim_{t \rightarrow \infty} \frac{g'_{21}(t)}{g_{21}(t)} &= \lim_{t \rightarrow \infty} \frac{[xe^{xt} - ye^{yt}]}{[e^{xt} - e^{yt}]} \\
&= \lim_{t \rightarrow \infty} \frac{x - ye^{(y-x)t}}{1 - e^{(y-x)t}}.
\end{aligned}$$

However,

$$y - x = \left[\frac{-b + c^2 - Q}{2c} \right] - \left[\frac{-b + c^2 + Q}{2c} \right] = \frac{-Q}{c} < 0$$

and

$$\lim_{t \rightarrow \infty} e^{(y-x)t} = 0.$$

Hence

$$\begin{aligned}\lim_{t \rightarrow \infty} \frac{g'_{11}(t)}{g_{11}(t)} &= \lim_{t \rightarrow \infty} \frac{Ux + Vy e^{(y-x)t}}{U + V e^{(y-x)t}} \\ &= x\end{aligned}$$

and

$$\begin{aligned}\lim_{t \rightarrow \infty} \frac{g'_{21}(t)}{g_{21}(t)} &= \lim_{t \rightarrow \infty} \frac{x - y e^{(y-x)t}}{1 - e^{(y-x)t}} \\ &= x.\end{aligned}$$

So for t sufficiently large, we have

$$\begin{aligned}g'_{11}(t) &\approx x(g_{11}(t)) \\ &= \left(\frac{-b + c^2 + Q}{2c}\right)g_{11}(t) \\ g'_{21}(t) &\approx x(g_{21}(t)) \\ &= \left(\frac{-b + c^2 + Q}{2c}\right)g_{21}(t)\end{aligned}$$

and thus

$$\begin{aligned}\frac{dV}{dt} &= g_{11}(0)\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(t)\right) + \int_0^t g'_{11}(t-u)\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(u)\right)du \\ &= e^0\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(t)\right) + \left(\frac{-b + c^2 + Q}{2c}\right) \int_0^t g_{11}(t-u)\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(u)\right)du \\ &= \left(c\frac{a}{b} + cI - \frac{c}{3}V^3(t)\right) + \left(\frac{-b + c^2 + Q}{2c}\right)V(t) \\ &= \left(\frac{-b + c^2 + Q}{2c}\right)V(t) - \frac{c}{3}V^3(t) + c\frac{a}{b} + cI.\end{aligned}$$

Similarly,

$$\begin{aligned}\frac{d\theta}{dt} &= g_{21}(0)\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(t)\right) + \int_0^t g'_{21}(t-u)\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(u)\right)du \\ &= 0\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(t)\right) + \left(\frac{-b + c^2 + Q}{2c}\right) \int_0^t g_{21}(t-u)\left(c\frac{a}{b} + cI - \frac{c}{3}V^3(u)\right)du \\ &= \left(\frac{-b + c^2 + Q}{2c}\right)\theta(t).\end{aligned}$$

Since the above equation for $\theta(t)$ is a simple differential equation, we can easily find its solution. The equation for the action potential $V(t)$ is nonlinear but finite, thus we apply Carleman embedding technique to get the approximate solution.

Following the scheme proposed by Carleman, we can set

$$\begin{aligned} y_0 &= 1 \\ y_1 &= V \\ y_2 &= V^2 \\ y_3 &= V^3 \\ &\vdots \\ y_n &= V^n \\ &\vdots \end{aligned}$$

It follows that

$$\frac{dy_n}{dt} = \frac{dV^n}{dt} = nV^{n-1} \frac{dV}{dt}$$

so that from the initial condition

$$y_1(0) = V(0) = V_0; y_n(0) = V_0^n$$

and

$$\begin{aligned} \frac{dy_n}{dt} &= nV^{n-1}(t) \left[\left(\frac{-b + c^2 + Q}{2c} \right) V(t) - \frac{c}{3} V^3(t) + c \left(\frac{a}{b} + I \right) \right] \\ &= \left(\frac{-b + c^2 + Q}{2c} \right) nV^n(t) - \frac{nc}{3} V^{n+2}(t) + \left(\frac{ca + cIb}{b} \right) nV^{n-1} \\ &= \left(\frac{-b + c^2 + Q}{2c} \right) ny_n - \frac{nc}{3} y_{n+2} + \left(\frac{ca + cIb}{b} \right) ny_{n-1}. \end{aligned}$$

For the sake of simplicity, we make the following substitution

$$A = \frac{-b + c^2 + Q}{2c}; B = \frac{ca + cIb}{b}.$$

Then we have

$$\frac{dy_n}{dt} = Bny_{n-1} + Any_n - \frac{nc}{3}y_{n+2}; n \geq 1.$$

The above recurrence equation can be written in matrix form as

$$\frac{d}{dt} \begin{bmatrix} y_0 \\ y_1 \\ y_2 \\ y_3 \\ y_4 \\ \vdots \\ y_n \\ \vdots \end{bmatrix} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & \dots & 0 \\ B & A & 0 & \frac{-c}{3} & 0 & 0 & 0 & 0 & \dots & 0 \\ 0 & 2B & 2A & 0 & \frac{-2c}{3} & 0 & 0 & 0 & \dots & 0 \\ 0 & 0 & 3B & 3A & 0 & -c & 0 & 0 & \dots & 0 \\ 0 & 0 & 0 & 4B & 4A & 0 & \frac{-4c}{3} & 0 & \dots & 0 \\ \vdots & & & & \ddots & \ddots & & & \ddots & \vdots \\ 0 & 0 & 0 & 0 & 0 & \dots & nB & nA & \dots & 0 \\ \vdots & & & & \vdots & \vdots & & \ddots & \ddots & \vdots \end{bmatrix} \begin{bmatrix} y_0 \\ y_1 \\ y_2 \\ y_3 \\ y_4 \\ \vdots \\ y_n \\ \vdots \end{bmatrix}.$$

We can write the above system in compact form as

$$\frac{dY}{dt} = MY. \quad (13)$$

The solution to equation (13) is given by

$$Y(t) = Y_0 e^{Mt} \quad (14)$$

where Y_0 is the initial value

$$Y_0 = \begin{bmatrix} y_0(0) \\ y_1(0) \\ y_2(0) \\ y_3(0) \\ y_4(0) \\ \vdots \\ y_n(0) \\ \vdots \end{bmatrix} = \begin{bmatrix} 1 \\ V_0 \\ V_0^2 \\ V_0^3 \\ V_0^4 \\ \vdots \\ V_0^n \\ \vdots \end{bmatrix}$$

Here we noticed that the two-dimensional Fitzhugh Nagumo equations are embedded into infinite nonlinear systems of differential equations. However, it is hard to find the closed form of the solutions of equation (13). Therefore, by truncating the matrix M at $n = 15$, one can use computer simulation to find the approximate solutions. Then we can compare the results obtained by numerical and Carleman embedding technique.

4 SIMULATION RESULTS

In this section, the two-dimensional Fitzhugh Nagumo system of ordinary differential equations are numerically integrated using Maple and we compared the results with the solution obtained by the Carleman Embedding Technique.

For the Carleman technique, the matrix is truncated at $n = 15$ and the code uses the parameter values of $a = 0.7, b = 0.8, c = 0.08, V_0 = 0.4$. For different initial values of the action potential $V(0)$, it can be seen that the system approaches to the same equilibrium point.

Three different values of the stimulus $I = -0.2, I = 0, I = 0.2$ are used to explore the solutions and predict corresponding activity of neurons.

In general, the following four issues are discussed.

1. Carleman Embedding Technique Solutions ,
2. Time Series and Equilibrium Points,
3. Effect of Changing Initial Conditions, and
4. Excitability.

4.1 Carleman Embedding Technique Solutions

Figure 5 compares the Carleman Embedding Technique to numerical solutions. The result is approximation to the solution of the Fitzhugh Nagumo equation and it can be used to approximate the solution of other systems of nonlinear differential equations.

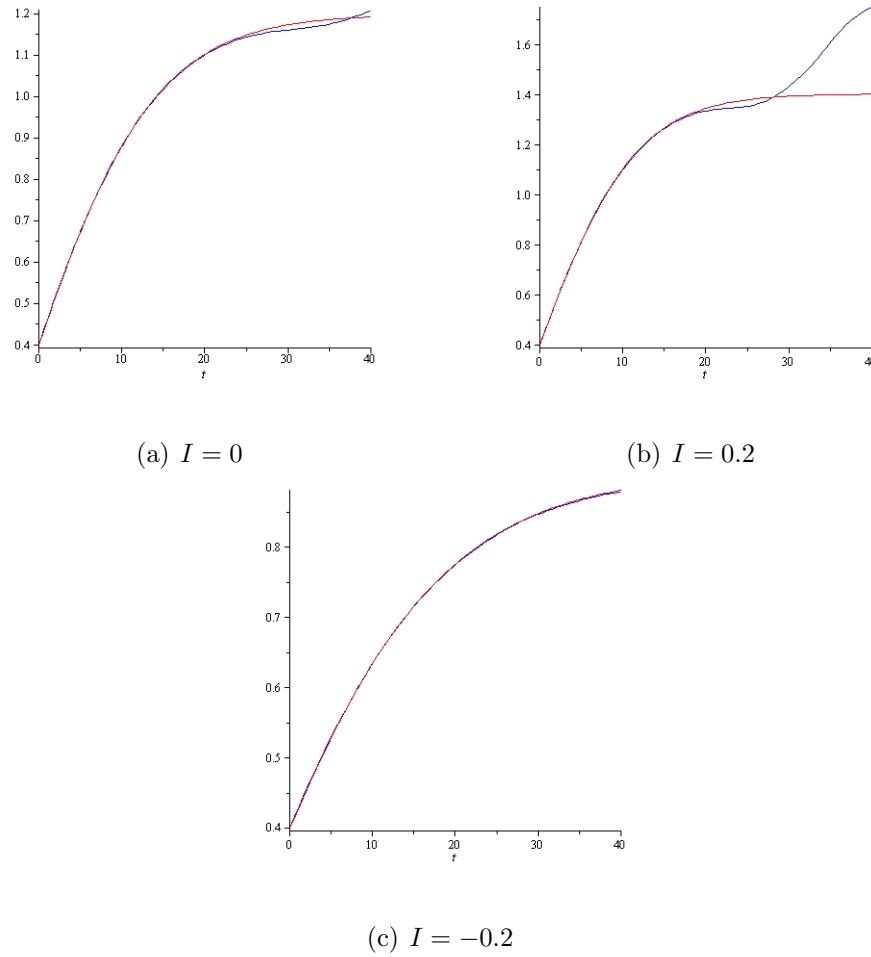


Figure 5: Comparison of Numerical and Carleman solutions for different I values

4.2 Time Series and Equilibrium Points

Figure 6 shows that V asymptotically approaches its equilibrium value of about 1.2 and W is monotonically approaching its steady state value of about -0.6. We thus know that there is a stable fixed point in the system at $(x, y) \approx (1.2, -0.6)$ [15]. We can confirm this by doing simple algebra with equation (10).

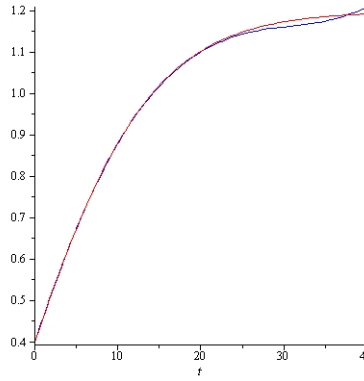


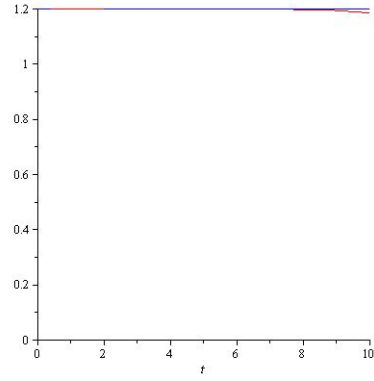
Figure 6: Solution using Numerical and Carleman, $I = 0$

4.3 Effect of Changing Initial Conditions

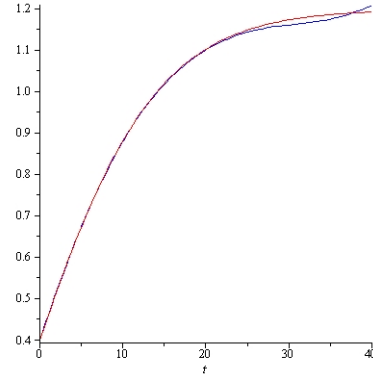
We can check whether this is the only stable fixed point present in the system. Using numerical integration, one can search for multiple fixed points by investigating what happens as the initial condition is changed in a systematic manner. If we change our initial condition from $V_0 = 0.4$ to $V_0 = 1.1994$ and run the simulation, we see the trace appears on the plot eventually approaches the same asymptotic or steady state value as before. If we continue modifying the initial condition, we can see that there

is only one fixed point in the system of equation (10).

If we set the initial conditions and find the equilibria algebraically, we see that the fixed point is stable and lies at $(x^*, y^*) = (1.1994, -0.62426)$ [15]. Figure 7 shows that, for different initial values of V_0 , the trace of the action potential asymptotically approaches the equilibrium point.



(a) $I = 0, V_0 = 0.4$



(b) $I = 0.2, V_0 = 1.1994$

Figure 7: Comparison of Numerical and Carleman solutions for different initial values of V_0

4.4 Excitability

The fact that small changes in initial conditions can have a large effect on the resultant trajectory is responsible for the property of excitability possessed by the FitzHugh-Nagumo equations [15]. We can see this by running the simulation for different values of the current.

1. For $I = 0$, $V_0 = 1.1994$, the trace is a horizontal line, since our initial condition is now at the fixed point itself: the transient previously present has evaporated. Figure 8 shows that if we don't inject a depolarizing current, the trace of the action potential remains horizontal [15].

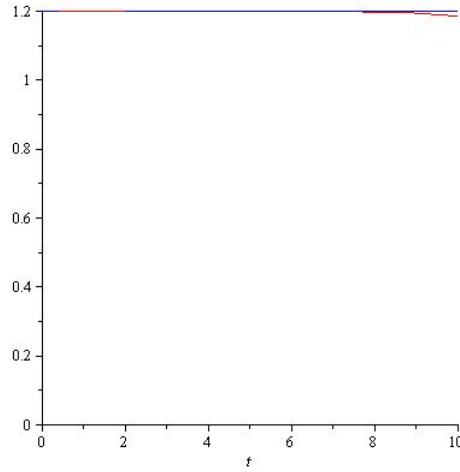


Figure 8: No threshold, $I=0$, $V_0 = 1.1994$

2. If we inject a strong depolarizing stimulus current of amplitude 2.0, we see that there is an action potential with a fast upstroke phase. Figure 9 illustrates that the trajectory of the action potential V moves away from the equilibrium point.

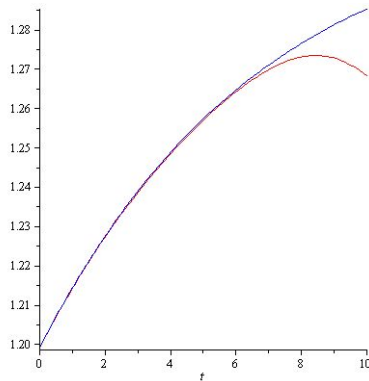


Figure 9: Suprathreshold, $I=0.2$, $V_0 = 1.1994$

3. If we change the stimulus amplitude to -2.0, we see the response of the subthreshold. Figure 10 shows that the trajectory of the action potential dies away quickly as a result of the negative current.

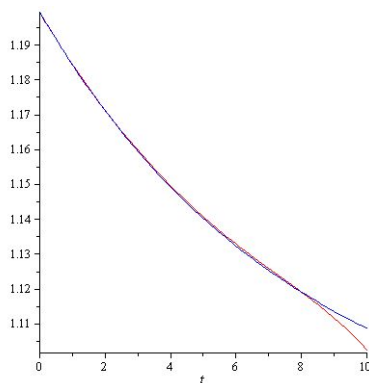


Figure 10: Subthreshold, $I=-0.2$, $V_0 = 1.1994$

4.5 Conclusion

It is known that finding the closed form of the solutions of nonlinear finite autonomous systems of differential equations is almost impossible [2]. It will, however, be approximated by using Carleman Embedding Technique. We have shown that the Carleman embedding technique can be applied to find the approximate solutions not only for those with periodic nature, but also for systems whose solutions are not periodic.

From the simulation results, it can be seen that the Carleman embedding technique did appear to have some practicality in finding the approximate solutions of Van der pol's equations and Fitzhugh Nagumo equations.

In the case of Fitzhugh Nagumo, we saw some differences between the Carleman solution and the numerical solution. This is due to the fact that we truncated the matrix at $n = 15$. But if we increase the dimension of the matrix moderately large, the technique will approximate the solution effectively.

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APPENDICES

APPENDIX A: The Matrix G

> with(LinearAlgebra):

M:=Matrix([[c,c],[-1/c,-b/c]]);

$$M := \begin{bmatrix} c & c \\ -\frac{1}{c} & -\frac{b}{c} \end{bmatrix} \quad (1)$$

> G := MatrixExponential(M*t);

$$G := \begin{bmatrix} \frac{1}{2} \frac{1}{\sqrt{b^2 + 2bc^2 + c^4 - 4c^2}} \left(e^{\frac{1}{2} \frac{(-b + c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} \right. \right. \quad (2)$$

$$\sqrt{b^2 + 2bc^2 + c^4 - 4c^2} - c^2 e^{-\frac{1}{2} \frac{(b - c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} \\ + c^2 e^{\frac{1}{2} \frac{(-b + c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} - b e^{-\frac{1}{2} \frac{(b - c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}}$$

$$+ b e^{\frac{1}{2} \frac{(-b + c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}}$$

$$\left. + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2} e^{-\frac{1}{2} \frac{(b - c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} \right),$$

$$\frac{c^2 \left(-e^{-\frac{1}{2} \frac{(b - c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} + e^{\frac{1}{2} \frac{(-b + c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} \right)}{\sqrt{b^2 + 2bc^2 + c^4 - 4c^2}} \Bigg],$$

$$\left[-\frac{-e^{-\frac{1}{2} \frac{(b - c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} + e^{\frac{1}{2} \frac{(-b + c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}}}{\sqrt{b^2 + 2bc^2 + c^4 - 4c^2}}, \right.$$

$$\begin{aligned} & \frac{1}{2} \frac{1}{\sqrt{b^2 + 2bc^2 + c^4 - 4c^2}} \left(e^{\frac{1}{2} \frac{(-b + c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} \right. \\ & \sqrt{b^2 + 2bc^2 + c^4 - 4c^2} + b e^{-\frac{1}{2} \frac{(b - c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} \\ & - b e^{\frac{1}{2} \frac{(-b + c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} + c^2 e^{-\frac{1}{2} \frac{(b - c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} \\ & - c^2 e^{\frac{1}{2} \frac{(-b + c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} \\ & \left. + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2} e^{-\frac{1}{2} \frac{(b - c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} \right) \Bigg] \end{aligned}$$

> g11 := G[1, 1];

g11 :=

(3)

$$\begin{aligned} & \frac{1}{2} \frac{1}{\sqrt{b^2 + 2bc^2 + c^4 - 4c^2}} \left(e^{\frac{1}{2} \frac{(-b + c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} \right. \\ & \sqrt{b^2 + 2bc^2 + c^4 - 4c^2} - c^2 e^{-\frac{1}{2} \frac{(b - c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} \\ & + c^2 e^{\frac{1}{2} \frac{(-b + c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} - b e^{-\frac{1}{2} \frac{(b - c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} \\ & + b e^{\frac{1}{2} \frac{(-b + c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} \\ & \left. + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2} e^{-\frac{1}{2} \frac{(b - c^2 + \sqrt{b^2 + 2bc^2 + c^4 - 4c^2})t}{c}} \right) \end{aligned}$$

> MM := Matrix([[[0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0], [B, A, 0, -1/3 c, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0], [0, 2·B, 2·A, 0, -2/3 c, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0], [0, 0, 3·B, 3·A, 0, -c, 0, 0, 0, 0, 0, 0, 0, 0, 0], [0, 0, 0, 4·B, 4·A, 0, -4/3 c, 0, 0, 0, 0, 0, 0, 0, 0], [0, 0, 0, 0, 5·B, 5·A, 0, -5/3 c, 0, 0, 0, 0, 0, 0, 0], [0, 0, 0, 0, 0, 6·B, 6·A, 0, -2·c, 0, 0, 0, 0, 0, 0], [0, 0, 0, 0, 0, 0, 7·B, 7·A, 0, -7/3 c, 0, 0, 0, 0, 0], [0, 0, 0, 0, 0, 0, 0, 8·B, 8·A, 0, -8/3 c, 0, 0, 0, 0], [0, 0, 0, 0, 0, 0, 0, 0, 9·B, 9·A, 0, -3 c, 0, 0, 0], [0, 0, 0, 0, 0, 0, 0, 0, 0, 10·B, 10·A, 0, -10/3 c, 0, 0], [0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 11·B, 11·A, 0, -11/3 c, 0], [0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 12·B, 12·A, 0, -4 c], [0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 13·B, 13·A, 0], [0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 14·B, 14·A]]) :

APPENDIX B: Maple Code

```

> M := subs(A = -0.02, B = 0.08*i+0.07, c = 0.08, MM);

for kk from -1 to 1 do

YY[kk] := MatrixExponential(subs(i = .4*kk, M)*t);

V0:=<1, .4, .4^2, .4^3, .4^4, .4^5, .4^6, .4^7, .4^8, .4^9, .4^10,
.4^11, .4^12, .4^13, .4^14>;

Y[kk] := YY[kk][2,].V0;

end do;

> for jj from -1 to 1 do

plot(Re(Y[jj]), t = 0 .. 40)

end do;

> with(plots);

for k from -1 to 1 do

sys3 := {x(0) = .4, y(0) = .4, diff(x(t), t) = 0.08*(x(t)+y(t)+.4*k-(1/3)*x(t)^3),
diff(y(t), t) = -(x(t)-.7+.8*y(t))/(0.08)};

p[k] := dsolve(sys3, type = numeric)

end do;

> for jj from -1 to 1 do

display(plot(Re(Y[jj]), t = 0 .. 40, color = blue),

odeplot(p[jj], [[t, x(t)]], 0 .. 40, color = red))

end do;

```


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